

From Skin To Within- Navigating concurrent endocrine & dermatological disease

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Conflicts Of Interest & Disclosures



- Ariane Neuber is a consultant for IDEXX & is owner of Hund Katze Haut, Veterinary dermatology referral practice in Germany (near Bonn)

- Yvonne McGrotty is an employee of IDEXX France and of AniCura France

- *The information contained herein is intended to provide general guidance only. As with any diagnosis or treatment, you should use clinical discretion with each patient based on a complete evaluation of the patient, including history, physical presentation, and complete laboratory data. With respect to any drug therapy or monitoring program, you should refer to product inserts for a complete description of dosages, indications, interactions, and cautions. Diagnosis and treatment decisions are the ultimate responsibility of the primary care veterinarian.*

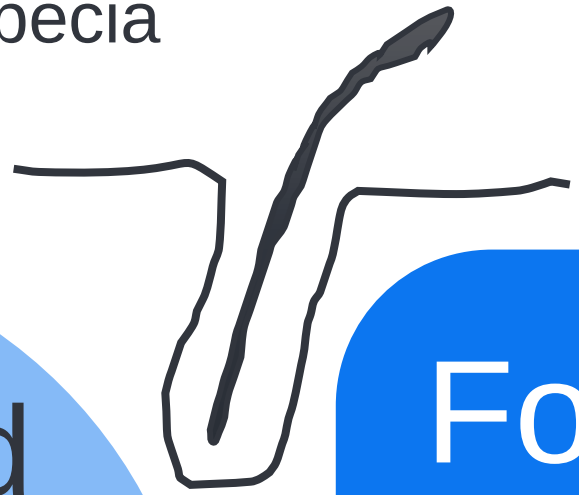
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Canine Alopecia. Frequent presenting sign

- Focal, multifocal, generalised
- Symmetrical vs asymmetrical
- Primary vs secondary
- Non-pruritic, pruritic
- Breed related
- Congenital, hereditary, aquired
- Inflammatory, non-inflammatory
- Colour related (CDA, BHFD)
- Cosmetic

- Infectious
- Auto-immune
- Neoplastic
- Parasitic
- Dysplastic
- Endocrine

Primary vs secondary alopecia



Hair pulled out (pruritus)→ traumatic = secundary

Folliculopathy (non-pruritic)→ hair falling out = primary

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Causes of alopecia

Primary

- Fungal
- Parasitic
- **Endocrine**
- Internal disease
- Neoplastic
- Autoimmune
- Nutritional deficiencies

Secondary

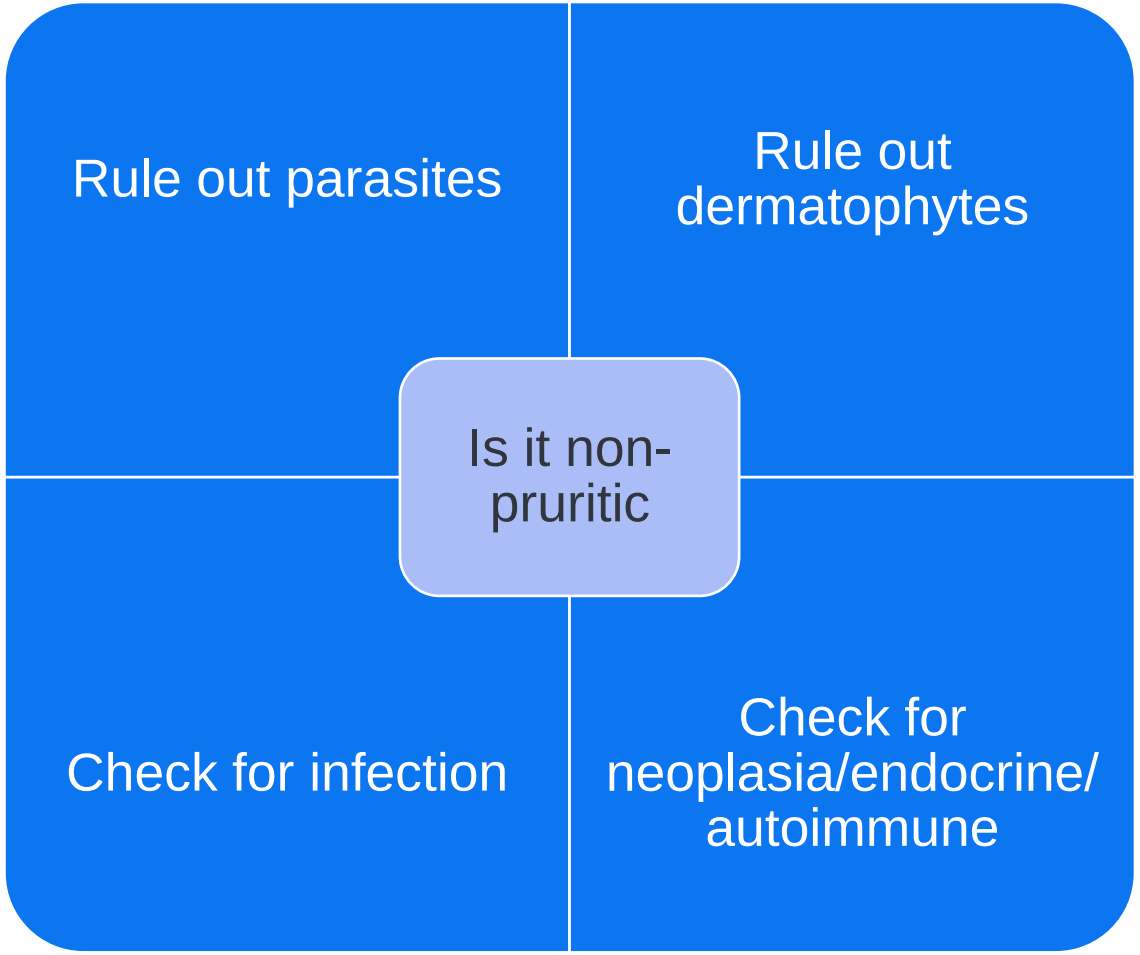
- Any disease causing pruritus, e.g.
  - Parasitic
  - Allergic
  - Neoplastic
  - Infection

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Approach

Is it pruritic?

- Rule out parasites
- Rule out dermatophytes
- Check for infection
- Check for neoplasia
- Is it an allergy ?



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Diagnostic tests

In house

- Skin scraping/Tape strip
- Cytology
- Fungal culture
- Ultrasound
- Diagnostic therapy (-laner)

Laboratory

- Fungal culture/PCR
- Histopathology
- Blood tests?

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Skin scraping

Needed:

- Good microscope
- Slides
- Scalpel blade,Mineral oil
- Clear tape
- Practice...expertise!



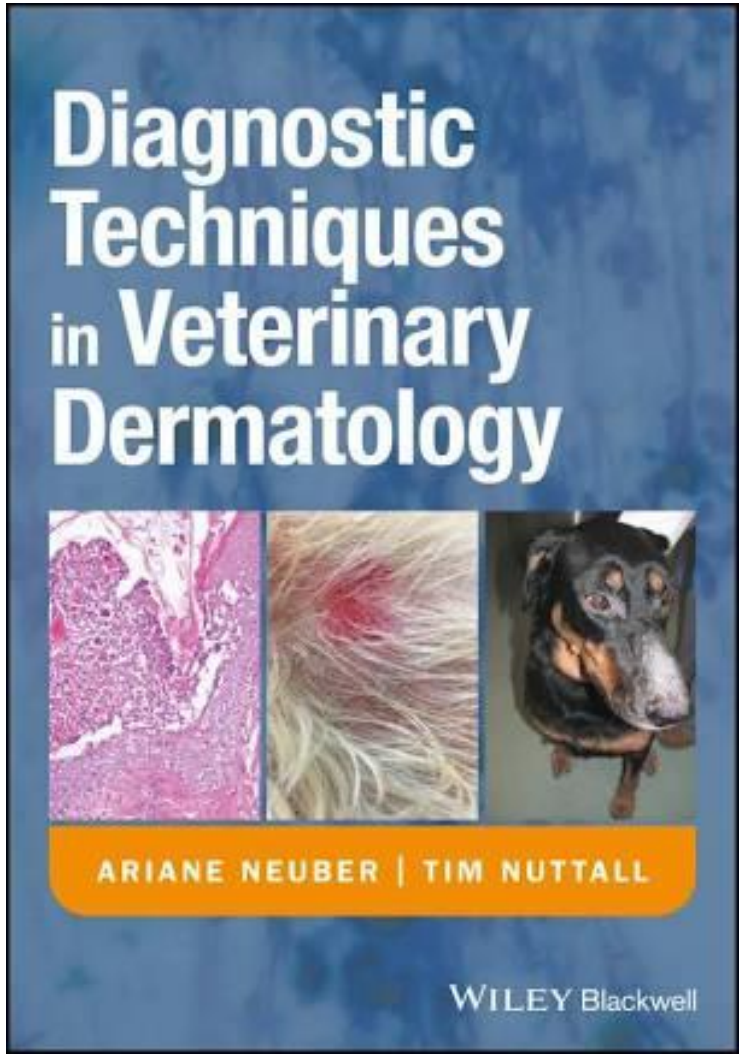
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Cytology

Needed:

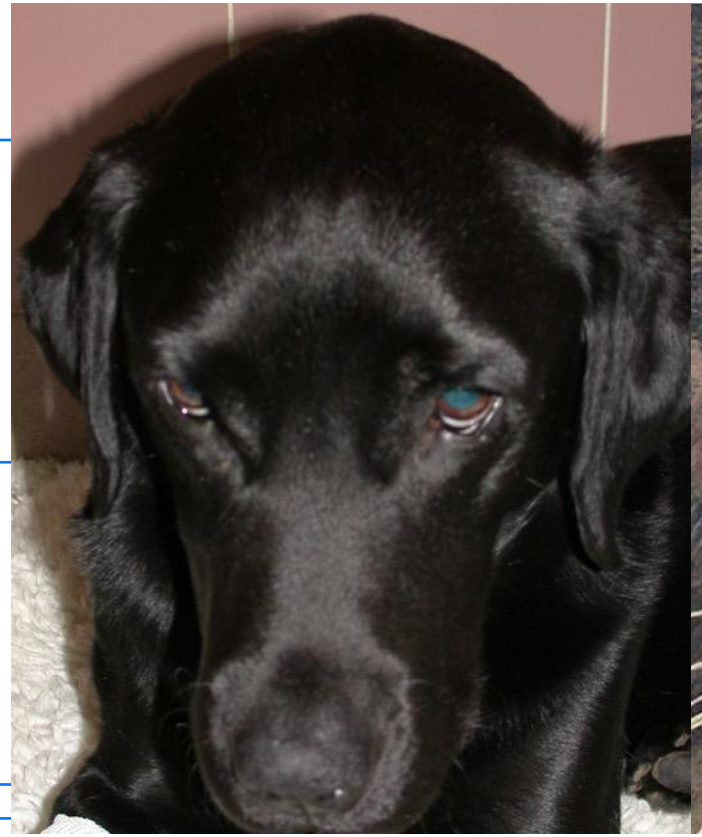
- Good microscope
- Slides
- Cotton buds
- Clear tape
- Stain (Romanovsky type)
- Practice...expertise!



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Which test is best?

The one that gives you an answer...





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Pruritic & inflammatory: CAD& dysbiosis





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Non pruritic & inflammatory: Demodex





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Endocrine immitators: Alopecia X





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Endocrine immitators seasonal flank alopecia

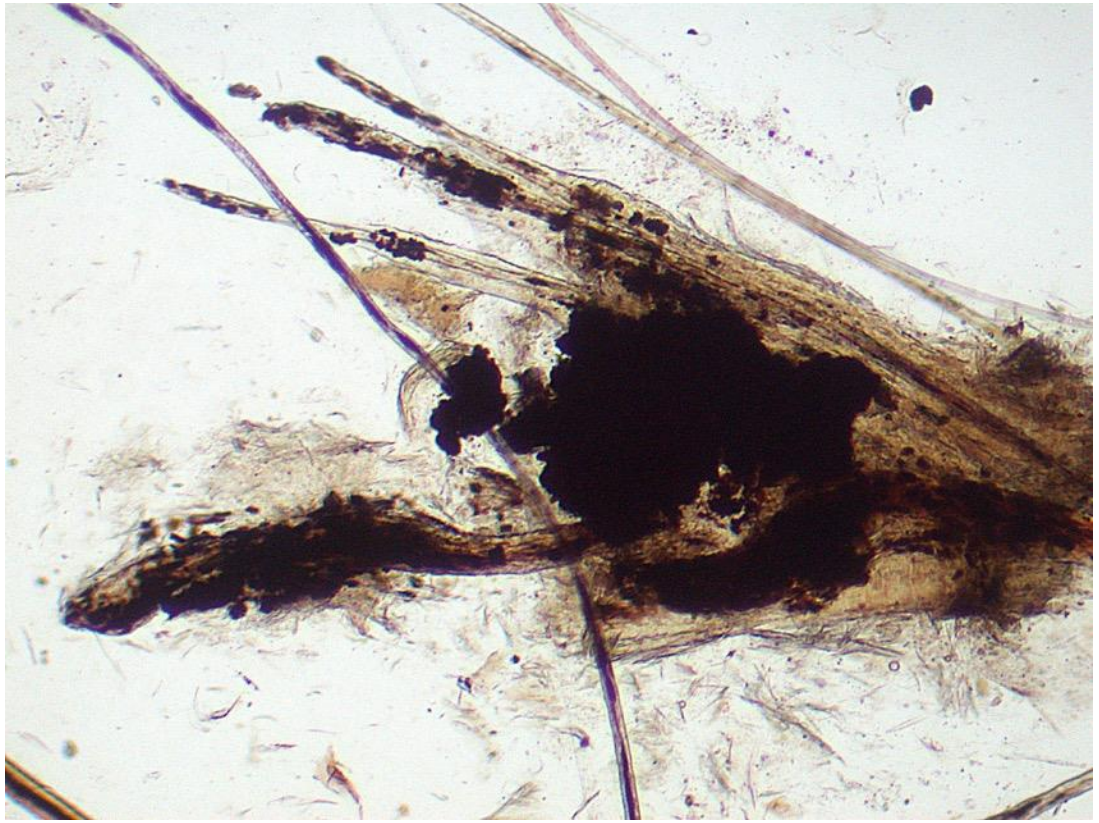




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Colour dilution alopecia

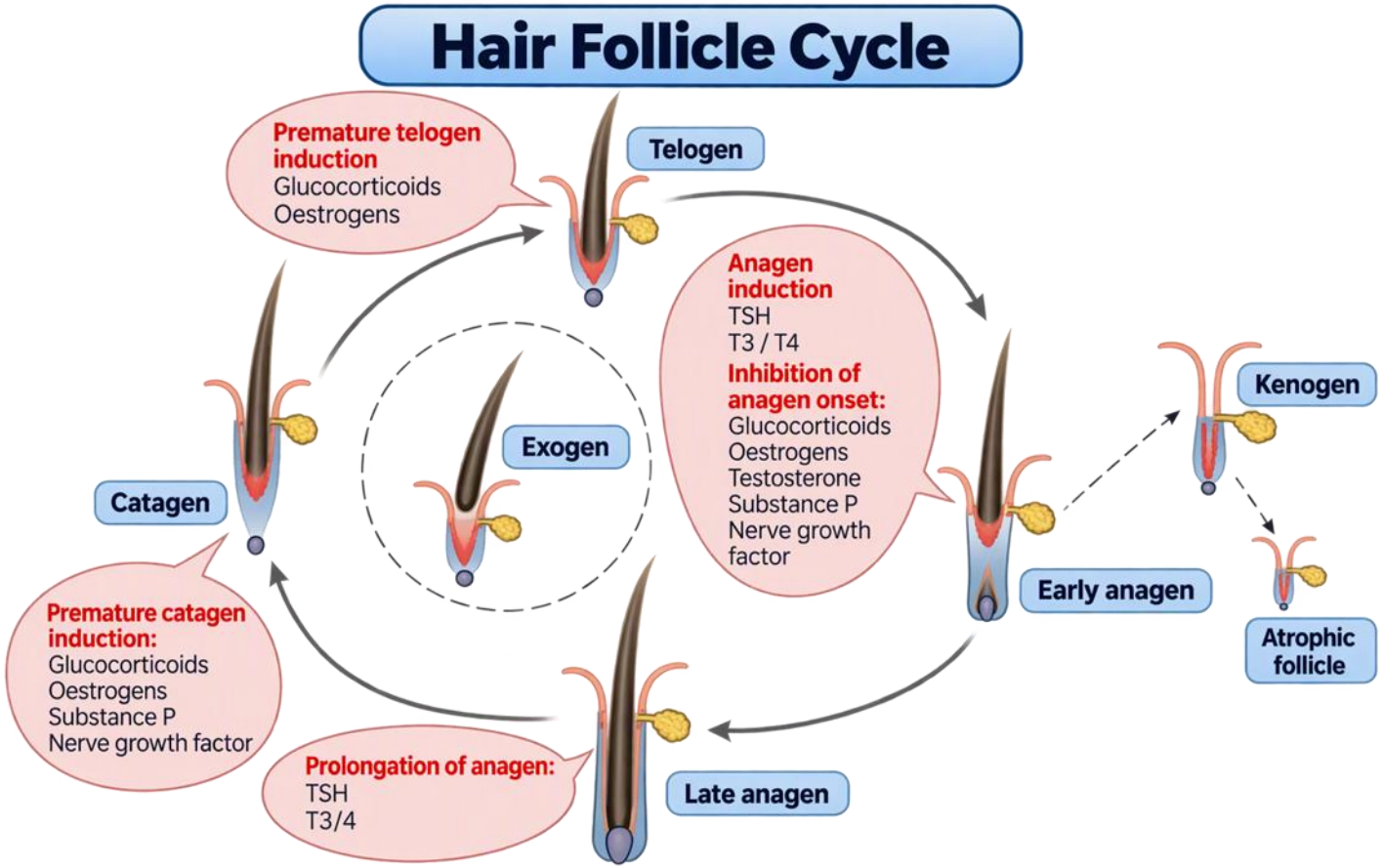




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What have the hormones ever done for the hair cycle?



AI modified, after Welle 2023

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Sertoli cell tumour





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Sertoli cell tumour





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Endocrine disease – cutaneous symptoms

Hypothyroidism

+ Dryness, dorsal scaling, excessive shedding, post clipping alopecia
+ hyperpigmentation
+ Nonpruritic bilateral symmetrical hypotrichia/alopecia (ventral & lateral trunk, caudal thighs, dorsal tail, ventral neck, dorsal nose)
+ Secondary pyoderma/dysbiosis → can lead to pruritus
+ Myxoedema (accumulation of glycosaminoglycans)→ forehead/face → tragic facial expression

Cushing's Syndrome

+ Non-pruritic, non inflammatory symmetrical truncal hypotrichia/ alopecia
+ Hypotonic (thin) skin
+ Comedones (ventral abdomen)
+ Dysbiosis (also otitis)
+ Calcinosis cutis
+ Changed hair color
+ Seborrhea oleosa
+ Poor wound healing
+ Demodicosis

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Hypothyroidism

Hypothyroid





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Hypothyroid





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How Do I Diagnose Primary Hypothyroidism In A Dog With Clinical Signs?

- Measure both TT4 and TSH
  - Low TT4 and increased TSH
  - Diagnostic



Total T4	10.0	13.0 - 51.0 nmol/L	
cTSH	0.64	0.00 - 0.50 ng/mL	

- T4 decreased but TSH WRI?
  - Measure FT4ED
    - Low FT4ED = diagnostic



High	†Cholesterol	10.96	mmol/L	3.20 - 6.20	
ENDOCRINOLOGY					
ALERT	TEST	RESULT	UNITS	REF.INTERVAL	
Low	Total T4	6.3	nmol/L	13.0 - 51.0	
Low	†Free T4 by ED (#)	<3.9	pmol/L	6.0 - 40.0	
	cTSH [a]	0.29	ng/mL	0.00 - 0.50	

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How To Monitor Response to Thyroxine Supplementation

- Start monitoring 4 weeks after starting supplementation
- Timing of blood sampling (peak)
  - Measure TT4 4-6hrs post pill
  - Except for Thyforon which is 3 hrs
- Measuring FT4 has no benefit for monitoring
- TSH can be measured but not necessary



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Thyroid Monitoring- Goals

+ Peak TT4 should be in upper half of ref range or slightly above it

†Total T4 [a]	57.8	nmol/L	13.0 - 51.0



+ If peak TT4 is less than 35nmol/l, increase dose

+ Increased TSH may also support need for higher dose
  + But not generally performed for monitoring



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Cushing’s Syndrome

Cushing‘s Syndrome



Photo- Ariane Neuber

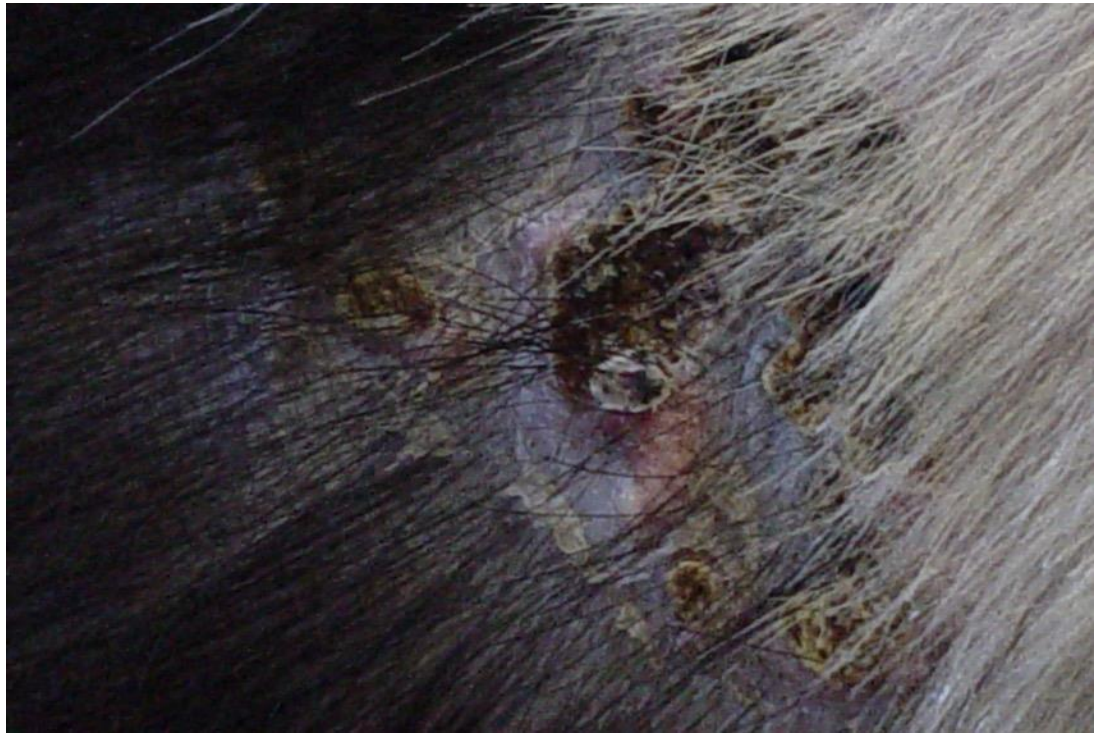


Photo -Yvonne McGrotty

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Calcinosis Cutis





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Diagnosing Cushing’s Syndrome

Diagnostic Approach To Suspected Cushing's

- History (including drug therapies)
- Quantify water intake accurately
  - Confirm PUPD

- Physical examination
- Urinalysis
- Haem/bio
- Specific endocrine tests
- Imaging



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First steps- Check for polydipsia/polydipsia

- Normal H_2O intake
  - 40-60mls/kg/day
- Polydipsia
  - >100 mls/kg/day in dogs
- Don’t test for HC in patients that aren’t PUPD
- Urine SG <1.020



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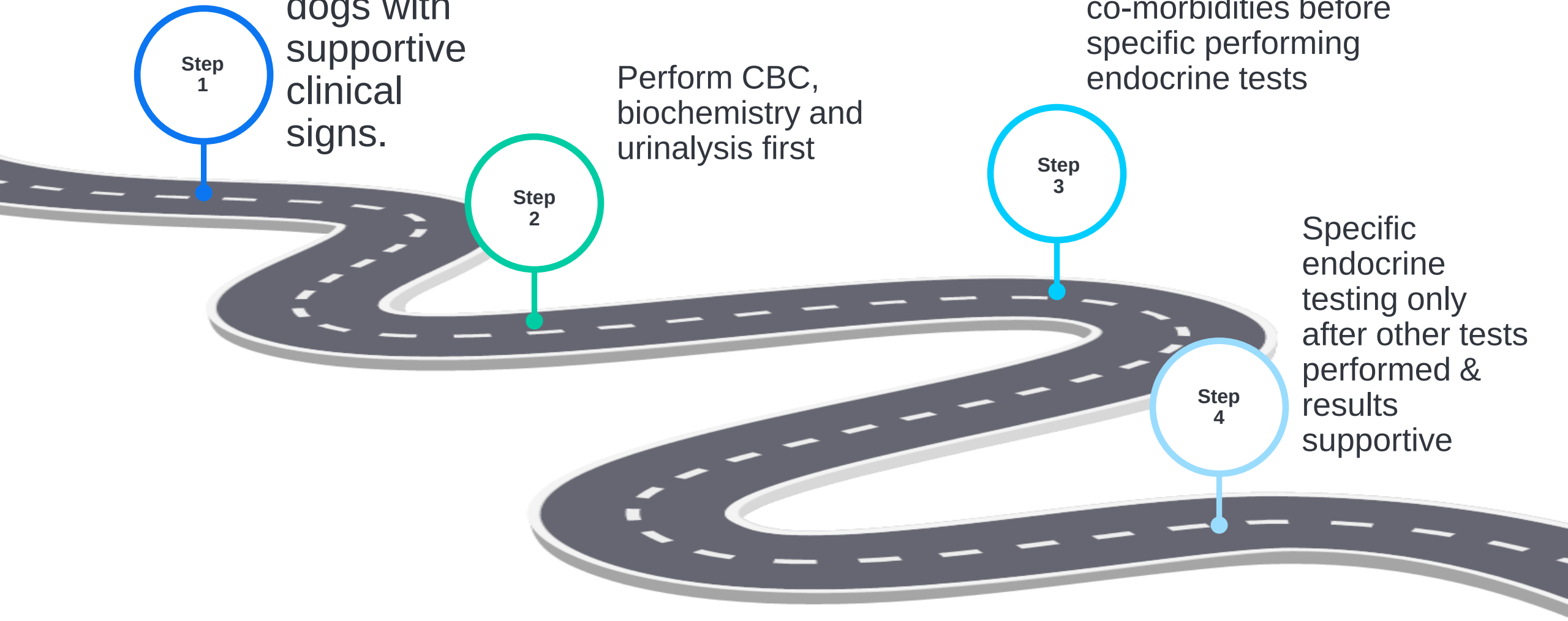
What is the best test to confirm Cushing's syndrome?

- Clinical signs!
  - PUPD
- Supportive clin path results
- Urinalysis confirming dilute urine
- Only then can you choose a more specific confirmatory test



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Cushing’s Syndrome- Testing Pathway



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Urine Cortisol:Creatinine (UCCR)

- Good screening test (rules out HC)
- Urine MUST be collected by owner at home
- False positives common
- Non-specific
- Positive result MUST be followed up by more specific testing

ACTH Stimulation Test Protocol

- Fast for 12hrs
- Sample for basal cortisol
- Inject tetracosactide (Cosacthen)
  - 5ug/kg IV
- Obtain 2nd sample 1hr later
- Measure cortisol on both samples



ACTH Stimulation Test- Problems

- Not all dogs with HC will test positive on ACTH stim
  - Only around 50% of dogs with ADH test positive
  - Around 80% of dogs with PDH test positive
- False negatives
  - Follow up with LDDST if HC still seems clinically likely
- False positives
  - Stress of non-adrenal illness (up to 14%)

Cortisol - Baseline	149.0	25.0 - 125.0 nmol/L	
Cortisol - Post ACTH	803.0	125.0 - 520.0 nmol/L	

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Low Dose Dexamethasone (LDDS) Test Protocol

- Fast the patient for 12 hours
- Sample for basal cortisol (T=0)
- Inject dexamethasone (0.015mg/kg) IV
- Sample for cortisol at 4hrs and 8hrs after dexamethasone injection
- Avoid stress for the duration of the test
  - No other procedures



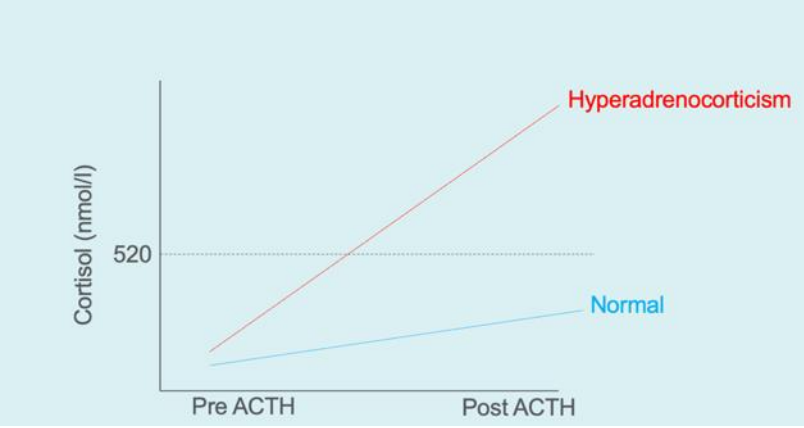
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Advantages & Disadvantages of LDDS

Advantages

+ Good screening test
  + 90-95% dogs with PDH test positive
  + Almost 100% ADH

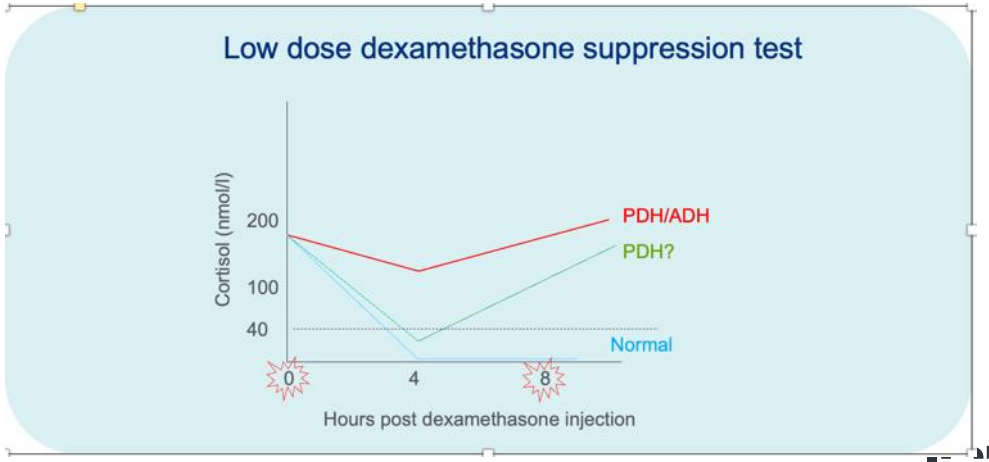
+ May confirm PDH
  + Suppression at 3-4hrs



Disadvantages

+ Low specificity
  + Especially in sick dogs (40-50%)
  + More likely to produce false positives

+ Takes longer to perform (8hrs)



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Comparison of ACTH stim & LDDS - Neither test is ideal!

ACTH Stim

- Quick test (1hr)
- Low sensitivity
  - High rate of false negatives
- Moderate risk of false positives
  - Especially diabetes mellitus
- Tests for iatrogenic HC

LDDS Test

- Long test (8hrs)
- High sensitivity
  - Low rate of false negatives
- Lower specificity
  - Risk of false positives
- Does not test for iatrogenic HC

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Treatment

Treatment of HC- Trilostane

- Competitive 3β hydroxysteroid dehydrogenase blocker
  - Blocks cortisol synthesis
  - Blocks sex hormones
  - Lesser effect on mineralocorticoids
- Well tolerated
- For both PDH & ADH
- Give with food
- Give in morning
  - To facilitate monitoring tests



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Monitoring Options For Cushing's Syndrome

ACTH Stimulation Test

- Perform 4-6hrs after pill
- Follow manufactuers guidelines
  - 10-14 days after starting or changing dose
- Aims:
  - Post-ACTH cortisol >40nmol/L but <200nmol/L

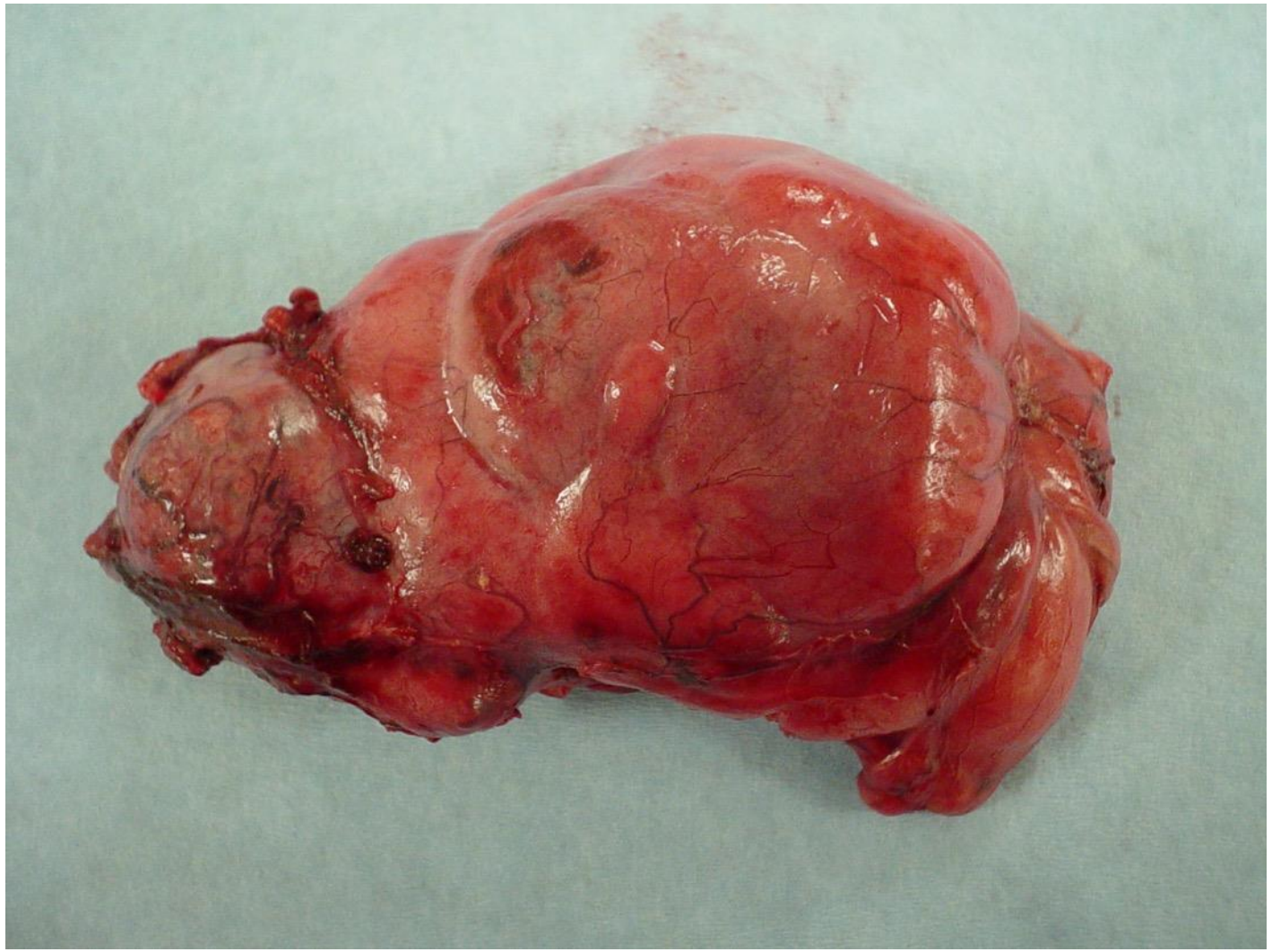
Pre-pill Cortisol

- Collect sample just before pill
- Not suitable for stressed/sick dogs
- Cortisol should be run at lab
- May still require follow-up ACTH stim

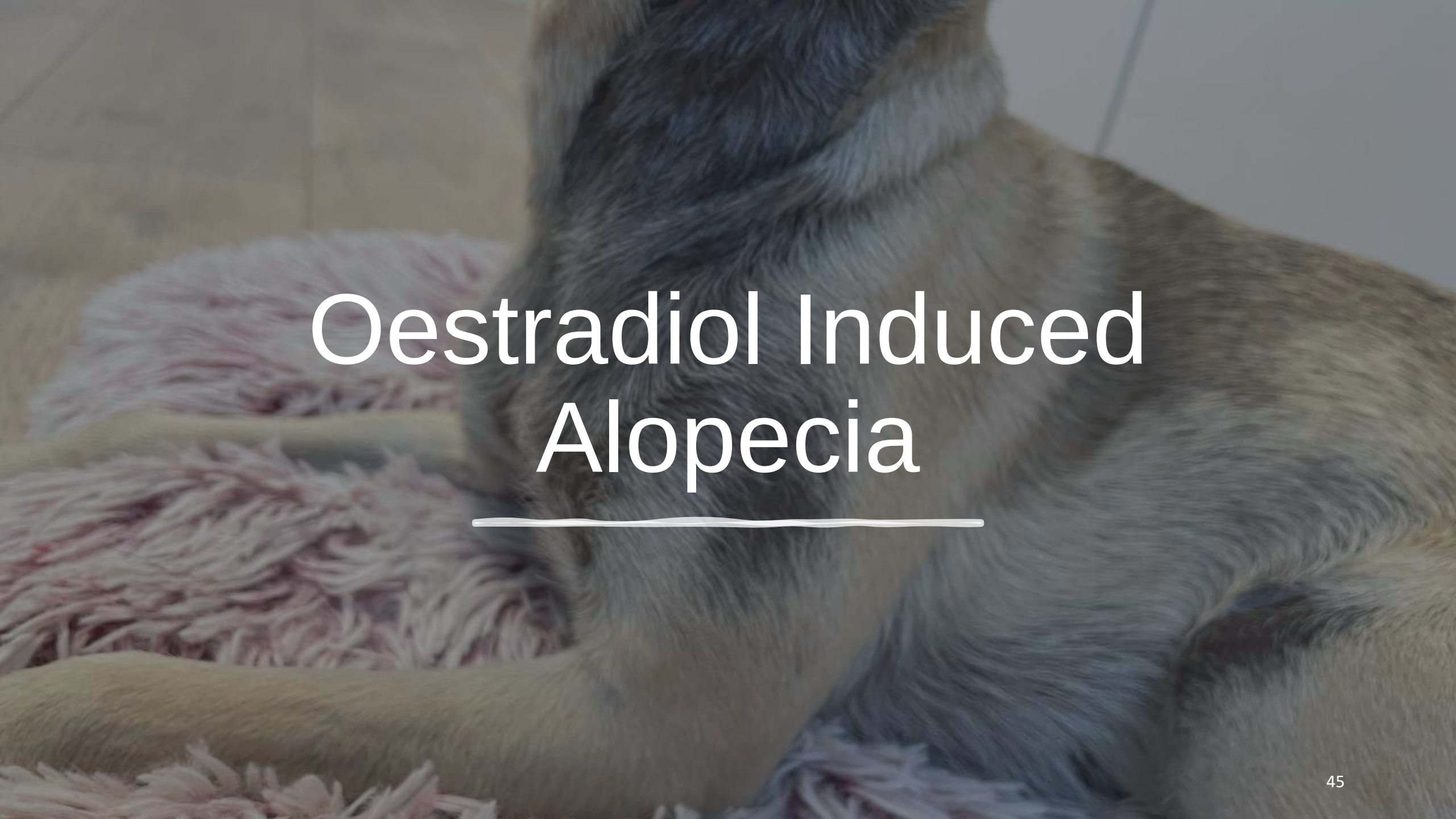
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Surgical Treatment

+ Adrenalectomy
+ Functional adrenal mass
+ Pre-op CT recommended



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Oestradiol Induced Alopecia

Menopause & HRT

+ HRT

+ More awareness...more medications

+ Topical preparations



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Risks & benefit analysis HRT (NHS website)

Relieving menopause symptoms

+ hot flushes
+ night sweats
+ sleep problems caused by menopause
+ anxiety and low mood caused by menopause
+ vaginal dryness

Preventing osteoporosis

Maintaining muscle strength

Breast cancer: little or no increase in the risk of breast cancer from oestrogen-only HRT

Blood clots: HRT patches, sprays and gels do not increase the risk

Stroke: tablets (but not patches, gel or spray) slightly increase the risk

Risks to pets & children

- FDA warning
- NHS/VMD warning

- Case reports:
- Stump pyometra spayed Chiahuahua
- Ovarian remnant syndrome
- Male cat mammary development, hyperoestrogenaemia, hypocortisolaemia

- Female pets: continuous oestrus
- (vaginal bleeding, swollen vulva)
- Pregnant bitches: birth defects
- Male pets: gynocomastia, changed testicular size
- Alopecia, behavioural changes, increased attentino 8from other pets9, reduced growth rate
- Bone marrow supression

Some publications

+ Wiener, D.J., Rüfenacht, S., Koch, H.J., Mauldin, E.A., Mayer, U. and Welle, M.M. (2015), Estradiol-induced alopecia in five dogs after contact with a transdermal gel used for the treatment of postmenopausal symptoms in women. Vet Dermatol, 26: 393-e91. https://doi.org/10.1111/vde.12242

+ Sjöström K, Mount J, Klocker A-K, Arthurson V. A review of adverse events in animals and children after secondary exposure to transdermal hormone-containing medicinal products. Vet Rec Open. 2022; 9:e48. https://doi.org/10.1002/vro2.48

6 m ME Rhodesian Ridgeback

- Symetrical alopecia
- Small testes, one retained
- Mammary hypertrocphy
- Preputial edge

- Cytology: preputium cellular keratinisation, (usually bitches in oestrus7hyperoestrogenism)
- Ultrasonography: small testes, normal structure
- non-detectable testosterone level & high oestradiol level
- 7 weeks post HRT withdrawal symütoms reduced

Dachshund puppies ME (3)

- Mammary hypertrophy, hypertrophied skin, alopecia ventral abdomen, hanging preputia & bilateral non-palpable testes
- HRT stopped
  - 1 year later puppies normal



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Cats (3)

- 3.5 y o Sphynx FN: exaggerated and persistent signs of oestrus (excessive vocalisation, decreased appetite, extra-affectionate behaviour and raised hindquarters → as general heath deteriorated PTS
- 2.5 yo MN Sphynx: anxiety, increased signs of territorialism and increased sexual interest
- 12 wk ME Spynx : significant enlargement of its mammary glands
- After HRT withdrawal cats made full recovery



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Diagnosis

+ Thorough history

+ Signalement often < 20kg

+ Clinical signs

+ Switch oral → gel/spray

+ Start medication



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Reduce risk – increase awareness!

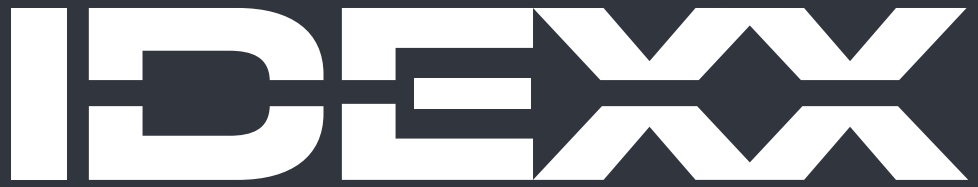
- Minimise pet‘s exposure to treated skin
- Wash hands with soap post application, pet not licking hand
- Cover application site (long sleever/trousers)
- Apply covered body site
- Wash application site after <2 (3) h gel, > 1 h spray
- Spray: not in same room as pet
- Apply at work (not if working with pets or children)
- Oral tx???



Regression of symptoms

- It depends...;)
- How long & much exposure
- Product used
- Coat density, breed, size
- Complete avoidance/reduction of exposure?





Any Questions?